

What is claimed is:

1. A method for administering nucleic acid to express a gene product in cells in tissue of interest, comprising:
treating the tissue to increase vascular permeability of exogenous nucleic acid;
and
administering exogenous nucleic acid to the tissue.
2. The method of claim 1 wherein the tissue is treated with a vascular permeability agent to increase vascular permeability.
3. The method of claim 1 or 2 wherein the nucleic acid is administered under low calcium ion concentration conditions.
4. The method of any one of claims 1-3 wherein the tissue is treated with a low calcium ion concentration solution.
5. A method for expressing a gene product in cells of tissue of interest, comprising:
treating the tissue with a vascular permeability agent under conditions of low calcium concentration to increase vascular permeability of exogenous nucleic acid;
and
administering exogenous nucleic acid to the tissue.
6. A method of any one of claims 1-5 wherein the nucleic acid is administered by perfusion.
7. The method of claim 6 wherein the perfusate of nucleic acid is recirculated and then readministered through the organ or cell mass.
8. The method of any one of claims 1-7 wherein the permeability agent is serotonin, bradykinin, platelet-activating factor, prostaglandin E₁, histamine, vascular endothelium growth factor, zona occludens toxin, interleukin-2, plasma kinins, L-N-monomethyl arginine or L-N-nitro-arginine methyl ester.
9. The method of claims 1-7 wherein the permeability agent is other than histamine.
10. The method of claims 1-7 wherein the permeability agent exhibits at least about 5% of the permeability activity of bradykinin in a standard permeability assay.

11. The method of any one of claims 1-10 wherein the permeability agent is perfused through vasculature of the tissue prior to administration of the nucleic acid.

12. The method of any one of claims 1-11 wherein a low calcium ion concentration solution is perfused through vasculature of the tissue prior to administration of the nucleic acid.

13. The method of any one of claims 1-12 wherein low calcium ion concentration conditions are provided by perfusing through vasculature of the tissue a fluid having a calcium ion concentration of from about 40 $\mu\text{mol/L}$ to about 500 $\mu\text{mol/L}$.

14. The method of any one of claims 1-13 wherein the nucleic acid is administered as a viral vector in a solution at a concentration of about 1×10^8 pfu/ml or greater.

15. The method of any one of claims 1-14 wherein the nucleic acid is administered to a solid cell mass.

16. The method of any one of claims 1-14 wherein the nucleic acid is administered to a solid organ.

17. The method of claims 1-14 wherein the nucleic acid is administered to cells of heart, lung, kidney, testes, ovaries, skeletal muscle, kidneys, brain or spleen.

18. The method of any one of claims 1-16 wherein the tissue is cardiac tissue.

19. The method of any one of claims 1-16 wherein the tissue is liver tissue.

20. The method of any one of claims 1-19 wherein the tissue comprises malignant cells.

21. The method of any one of claims 1-19 wherein the nucleic acid is administered to a solid tumor.

22. The method of any one of claims 1-21 wherein the tissue is mammalian.

23. The method of any one of claims 1-22 wherein the nucleic acid is administered *ex vivo*.

24. The method of any one of claims 1-22 wherein the nucleic acid is administered *in vivo*.

25. The method of any one of claims 1-24 wherein the nucleic acid is administered to a human.

26. The method of any one of claims 1-24 wherein the nucleic acid is administered to livestock, poultry or dog or cat.

27. A method for expressing a gene product in malignant cells in targeted tissue, comprising:

treating the tissue to increase vascular permeability of exogenous nucleic acid;
and

administering exogenous nucleic acid to the tissue.

28. The method of claim 27 wherein the tissue is treated with a vascular permeability agent to increase vascular permeability.

29. The method of claims 27 or 28 wherein the nucleic acid is administered under low calcium ion concentration conditions.

30. The method of any one of claims 27-29 wherein the nucleic acid is administered under low calcium ion concentration conditions.

31. The method of any one of claims 27-29 wherein a solid tumor comprises the malignant cells.

32. The method of any one of claims 27-31 wherein the malignant cells are present in a lung, liver, prostate, brain, testes or ovaries of a subject.

33. The method of any one of claims 27-32 wherein the nucleic acid is administered by perfusion.

34. The method of any one of claims 27-33 wherein the nucleic acid is administered to a mammal.

35. The method of any one of claims 27-33 wherein the nucleic acid is administered to a primate.

36. The method of any one of claims 27-33 wherein the nucleic acid is administered to a human.

37. A method of providing, to a recipient subject, donor cells that comprise nucleic acid exogenous to the cells, comprising:

treating tissue comprising the donor cells to increase vascular permeability of exogenous nucleic acid;

administering nucleic acid to the tissue; and

introducing the donor cells into the recipient subject to express a gene product of the nucleic acid.

38. The method of claim 37 wherein an organ comprising the donor cells is transplanted into the recipient subject.

39. The method of claim 37 wherein the donor cells are swine cells or primate cells.

40. The method of any one of claims 37-39 wherein the tissue is treated with a vascular permeability agent to increase vascular permeability.

41. The method of any one of claims 37-40 wherein the tissue is treated with a low calcium ion concentration solution to increase vascular permeability.

42. The method of any one of claims 37-41 wherein the nucleic acid is administered under low calcium ion concentration conditions.

43. The method of any one of claims 37-42 wherein the gene product reduces recognition of the donor cells by the immune system of the recipient subject.

44. The method of any one of claims 37-43 wherein the donor cells are introduced into a mammal.

45. The method of any one of claims 37-43 wherein the donor cells are introduced into a mammal.

46. The method of any one of claims 37-43 wherein the donor cells are introduced into a human.

47. A pharmaceutical kit comprising:
a permeability agent that can increase vascular permeability of a subject; and
nucleic acid for administration to a subject.

48. The kit of claim 47 further comprising a solution having a calcium ion concentration of from about 40 $\mu\text{mol/L}$ to about 500 $\mu\text{mol/L}$.

49. The kit of claim 47 or 48 further comprising a device for delivery of the nucleic acid.

50. The kit of claim 49 wherein the delivery device is a catheter.

51. The kit of any one of claims 47-50 wherein the nucleic acid is present in the kit as a viral vector.

52. A treatment solution comprising:

a) a permeability agent that can increase vascular permeability of nucleic acid; and

b) nucleic acid.

53. The treatment solution of claim 52 wherein the solution has a low calcium ion concentration.

54. The treatment solution of claim 53 wherein the solution has a calcium ion concentration of from about 40 $\mu\text{mol/L}$ to about 500 $\mu\text{mol/L}$.

55. A treatment solution comprising nucleic acid in a fluid carrier and having a low calcium ion concentration.

56. The treatment solution of claim 55 wherein the solution has a calcium ion concentration of from about 40 $\mu\text{mol/L}$ to about 500 $\mu\text{mol/L}$.

57. A solution of any one of claims 37-41 wherein the solution is pharmaceutically acceptable.

58. A solution of any one of claims 52-57 wherein the solution comprises one or more therapeutic agents in addition to the nucleic acid.

59. A solution of any one of claims 52-54 and 57-58 wherein the solution comprises a plurality of permeability agents.

60. A solution of any one of claims 52-54 and 57-58 wherein the permeability agent is serotonin, bradykinin, platelet-activating factor, prostaglandin E_1 , histamine, vascular endothelium growth factor, zona occludens toxin, interleukin-2, plasma kinins, L-N-monomethyl arginine or L-N-nitro-arginine methyl ester.